BIOGRAPHICAL SKETCH

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NAME: Michael C. Schmale, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): mschmale

POSITION TITLE: Professor of Marine Biology and Ecology, Associate Dean for Infrastructure

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date MM/YYYY	FIELD OF STUDY
Cornell University, Ithaca, NY	BA	05/1976	Biology
University of Miami, Miami, FL	MS	12/1979	Biological Oceanography
University of Miami, Miami, FL	PhD	05/1985	Biological Oceanography

A. Personal Statement

My research expertise is in the area of marine biomedical research and specifically aquatic animal models of human disease. In addition to Aplysia, I work with damselfish and zebrafish based models, as described below. I have been the Director of the National Resource for Aplysia and the PI on the P40 grant since 2006. Before that I was a Co-PI, dating back to the initial development of the Resource. My role is to coordinate all aspects of production and applied research, to help set priorities for the research programs, convene meetings of our External Advisory Board and interact with the community of users of our animals to determine that we are meeting their needs and to attempt to assess future needs. In addition, I supervise the animal health monitoring program and coordinate with the attending veterinarian, if necessary. My interests in Aplysia include developing Aplysia as a model of aging via a close collaboration with professor Fieber and her graduate students. I have focused my research efforts there on trying to understand metabolic pathways that may be significantly altered in aging in Aplysia using RNAseq and the Ingenuity Pathway Analysis platform to model these changes. In addition, I have conducting intensive investigations of a novel nidovirus (Aplysia Abyssovirus - AAbV) recently identified in transcriptome databases of Aplysia californica. We have determined using gPCR and RNAseq that AAbV load in Aplysia neurons increases with age and can reach extremely high levels in the nervous systems of aged animals, that the virus occurs at high levels in many wild-collected animals, and that this virus is vertically transmitted to eggs and larvae and there can interfere with normal larval development. I am supervising all aspects of viral assays including assay development and data interpretation.

Kron, N.S., Fieber, L.A., Baker, L., Campbell, C., and M.C. Schmale. 2024a Host response of Aplysia Abyssovirus 1 in nervous system and gill. Dev. Comp. Immunol. 159:1005211. <u>https://doi.org/10.1016/j.dci.2024.105211</u> PMID: 38885747

Kron, N.S., Neuman, B.W., Kumar, S., Blackwelder, P.L. Vidal, D., Fieber, L.A., and M.C. Schmale. 2024b. Expression dynamics of the Aplysia abyssovirus. Virology, 589 109890 <u>https://doi.org/10.1016/j.virol.2023.109890</u> PMID: 37951086

- Badal KK, Sadhu A, Raveendra BL, McCracken C, Lozano-Villada S, Shetty AC, Gillette P, Zhao Y, Stommes D, Fieber LA, Schmale MC, Mahurkar A, Hawkins RD, Puthanveettil SV. 2024 Single-neuron analysis of aging-associated changes in learning reveals impairments in transcriptional plasticity. Aging Cell. 2024 Sep;23(9):e14228. doi: 10.1111/acel.14228.
- Kron, N.S., Schmale, M.C., and L.A. Fieber (2020) Changes in metabolism and proteostasis drive aging phenotype in Aplysia californica sensory neurons. Front. Aging Neurosci, 12:280. Doi: 10.3389/fnagi.2020.573764, PMID: 33101008
- Greer, J. B., Schmale, M. C., & Fieber, L. A. (2018). Whole-transcriptome changes in gene expression accompany aging of sensory neurons in Aplysia californica. BMC Genomics. 2018 Jul 11;19(1):529. doi: 10.1186/s12864-018-4909-1.PMID: 29996779

B. Positions, Scientific Appointments, and Honors

Associate Dean for Infrastructure, RSMAS
Director, The National Resource for Aplysia, RSMAS
Professor; Division of Marine Biology and Fisheries, RSMAS
Associate Professor; Division of Marine Biology and Fisheries, RSMAS
Member: Interdepartmental Neuroscience Program, University of Miami
Assistant Professor; Division of Marine Biology and Fisheries, RSMAS
Research Assistant Professor; Division of Biology and Living Resources, RSMAS
Research Associate; Division of Biology and Living Resources, Rosenstiel School of Marine and Atmospheric Science, University of Miami (RSMAS)

Honors & Service

NIH Comparative Medicine Review Committee, Member 2003 – 2008 (Chair 2006 – 2008) Knight Molecular Biology Fellowship, 1998-1999 N.I.H. New Investigator Research Award, 1985 - 1988 F.G. Walton Smith Dissertation Prize, 1985

C. Contributions to Science

One of my major research foci for the past 20+ years has been on a naturally occurring cancer found in a species of reef fish, the bicolor damselfish (*Stegates partitus*), which I discovered in the 1980's on Florida reefs. This disease, termed damselfish neurofibromatosis, consists of multifocal neurofibromas, malignant peripheral nerve sheath tumors and chromatophoromas. We have been able to demonstrate that these tumors are infectious, transmissible by sub-cellular filtrates, and that the etiological agent is a novel type of virus-like agent which infects the mitochondria of the tumor cells. This agent is has a 2.4 kb circular DNA genome and is the first known pathogen of any type to replicate within the mitochondria of an animal cell. My laboratory has been investigating the life cycle of this agent and how it alters mitochondrial and cellular functions to result in tumorigenesis. We are currently using RNAseq to investigate changes in gene expression in cells from peripheral nerve sheath tumors and chromatophoromas in this disease.

- MC Schmale, PDL Gibbs, JJ Rahn, D Vidal, R Naviaux (2011) A virus-like agent in the mitochondria of bicolor damselfish. Mitochondrion 11 (4), 656. doi.org/10.1016/j.mito.2011.03.064
- Rahn, J.J., P.D.L Gibbs and M.C. Schmale. (2004) Patterns of Transcription of a Virus-Like Agent in Tumor and Non-Tumor Tissues in Bicolor Damselfish. Comp Biochem Physiol C 138: 401-409.
- Schmale, M.C., P.D.L. Gibbs and C.E. Campbell (2002) A virus-like agent associated with neurofibromatosis in damselfish. Diseases Aquatic Organisms 49:107-115.
- Campbell, C.E. and M.C. Schmale (2001) Distribution of a novel infectious agent in healthy and tumored bicolor damselfish in Florida and the Caribbean. Marine Biology 139:777-786.

My laboratory been very active in development and application of the zebrafish embryo model system for investigation of the toxic effects of harmful algal blooms (HABs) and for bioassay guided fractionation to identify specific toxin molecules from these complex mixtures. This research is based on an ongoing collaboration for over 15 years with Prof. John Berry at Florida International University. My laboratory has worked with John to develop and optimize assays based on exposure of zebrafish embryos to HAB components as a means to both characterize specific developmental abnormalities (which we term "toxitypes") and to use these responses to drive the fractionation of HAB components by a process dubbed bioassay guided fractionation. This stepwise process, conducted as a close collaboration between Dr. Berry's laboratory at FIU and Dr. Pat Gibbs in my laboratory, has allowed identification of specific toxin molecules from complex HAB-derived mixtures. My laboratory maintains a zebrafish colony where we regularly breed a number of lines including several transgenic lines which have been useful in HAB assays, carry out embryo exposures and characterize developmental abnormalities. We also host a shared microscopy resource which is ideal for monitoring and imaging of zebrafish embryos.

- Jaja-Chimedza A, Sanchez K, Gantar M, Gibbs P, Schmale M, Berry JP (2017) Carotenoid glycosides from cyanobacteria are teratogenic in the zebrafish (Danio rerio) embryo model. Chemosphere 174:478-489. doi: 10.1016/j.chemosphere.2017.01.145. PMID: 28189893
- Walton K, Gantar M, Gibbs PD, Schmale MC, Berry JP. (2014) Indole alkaloids from Fischerella inhibit vertebrate development in the zebrafish (Danio rerio) embryo model. Toxins.; 6(12):3568-81. PubMed [journal] PMID: 25533520, PMCID: PMC4280548
- Jaja-Chimedza A, Gantar M, Gibbs PDL, Schmale MC, Berry JP. (2012) Polymethoxy-1-alkenes from Aphanizomenon ovalisporum inhibit vertebrate development in the zebrafish (Danio rerio) embryo model. Mar Drugs. Oct;10(10):2322-2336. doi: 10.3390/md10102322. Epub 2012 Oct 22. PMID: 23170087
- Berry, J.P., M. Gantar, P.D.L Gibbs, and M.C. Schmale (2007) The Zebrafish (Danio rerio) Embryo as a Model System for Identification and Characterization of Developmental Toxins from Marine and Freshwater Microalgae. Comp Biochem Physiol Part C 145:61–72.

In addition, my laboratory has been active in developing and employing a several of transgenic lines of zebrafish to address a variety of research questions. We isolated and further developed two unique fluorescent protein (FP) molecules from two species of corals which we subsequently patented. These FPs have proven very useful in creating effective transgenic constructs. Much of this work has been directed toward developing transgenic zebrafish which are able to detect toxin molecules in the water. We have created lines with methallothonein promoters driving green FPs which are very responsive to low levels of mercury (50 nM), lead (<1 uM) and other heavy metals. We also have produced lines with heat shock, ubiquitin and p450-like promoters. We continue to develop such transgenic fish with the idea of creating sensitive bio-indicators of HAB toxins.

- Carter, R., M.C. Schmale, and P.D.L. Gibbs. (2004) Cloning of Anthozoan Fluorescent Protein Genes. Comp Biochem Physiol C 138:259-270.
- Gibbs, P.D.L. & M.C. Schmale (2000) GFP as a genetic marker scorable throughout the lifecycle of transgenic zebrafish. Marine Biotechnology 2:107-125.
- Gibbs, P.D.L., R. Carter and M.C. Schmale (2008) United States Patent 7,413,874 -. Nucleic acid encoding fluorescent proteins from aquatic species. Issued August 19, 2008.
- Gibbs, P.D.L., R. Carter and M.C. Schmale (2007) United States Patent 7,291,711 -. Fluorescent proteins from aquatic species. Issued November 6, 2007.

Finally, I have long history of involvement in organizing conferences revolving around the development and application of aquatic animal models for the study of human disease. These have resulted in many white papers summarizing the state of the field as well as prospects and priorities for future research initiatives.

- Hinton DE, Hardman RC, Kullman SW, Law JM, Schmale MC, Walter RB, Winn RN, Yoder JA (2009) Aquatic animal models of human disease: selected papers and recommendations from the 4th Conference. Comp Biochem Physiol C Toxicol Pharmacol. Mar;149(2):121-8. doi: 10.1016/j.cbpc.2008.12.006. Epub 2008 Dec 24. PMID: 19150511
- Schmale MC, Nairn RS, Winn RN (2007) Aquatic animal models of human disease. Comp Biochem Physiol C Toxicol Pharmacol. Feb;145(1):1-4. doi: 10.1016/j.cbpc.2006.11.013. Epub 2006 Dec 6. PMID: 17198764
- Nairn RS, Schmale MC, Stegman J, Winn RN, Walter RB (2001) Aquaria fish models of human disease: reports and recommendations from the working groups. Mar Biotechnol (NY). Jun;3(Supplement 1):S249-58. doi: 10.1007/s10126-001-0047-9. PMID: 14961321